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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,251	10/20/2006	Luca Gianni	13566.105020	7104

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EXAMINER	
LAU, JONATHAN S	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/579,251	GIANNI ET AL.	
	Examiner	Art Unit	
	Jonathan S. Lau	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5 pgs / 28 Apr 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is responsive to Applicant's Amendment and Remarks, filed 28 Apr 2008, in which claims 2, 11 and 16-19 are canceled; claims 1 and 10 are amended to change the scope and breadth of the claim; and claims 3, 12 and 13 are amended so as not to depend from a canceled claim.

This application is the national stage entry of PCT/GB04/50025, filed 12 Nov 2004; and claims benefit of foreign priority document UNITED KINGDOM 0326486.8, filed 14 Nov 2003. The foreign priority document is in English.

Claims 1, 3-10 and 12-15 are pending.

Objections Withdrawn

Applicant's Amendment, filed 28 Apr 2008, with respect to objections to the specification has been fully considered and is persuasive, as it is now clear that the abbreviations "Doxo" and "doxo" define the same term.

This objection has been **withdrawn**.

Rejections Withdrawn

Applicant's Amendment, filed 28 Apr 2008, with respect to rejection of claims 1, 3-8, 11, 14, 15 and 19 under 35 U.S.C. 102(b) as being anticipated by Takahashi et al. (WIPO publication WO 02/36135, published 10 May 2002, of record) and Bowman et al.

(WIPO publication WO 00/69441, published 23 Nov 2000, of record), which is incorporated-by-reference into Takahashi et al. (Takahashi et al. page 1, lines 5-7), has been fully considered and is persuasive, as Takahashi et al. does not specifically disclose doxorubicin administered with a dose of about 60 mg/m^2 or about 50 mg/m^2.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 28 Apr 2008, with respect to rejection of claims 1, 3 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 33 and 34 of copending Application No. 09/787,461, has been fully considered and is persuasive, as Application No. 09/787,461 does not specifically disclose doxorubicin administered with a dose of about 60 mg/m^2 or about 50 mg/m^2.

This rejection has been **withdrawn**.

Applicant's Amendment, filed 28 Apr 2008, with respect to rejection of claims 1-9 and 19 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 19-20 of copending Application No. 11/577,790, has been fully considered and is persuasive with regard to claims 2 and 19, as claims 2 and 19 are canceled.

This rejection of claims 2 and 19 has been **withdrawn**. This rejection of claims 1 and 3-9 is modified as recited below.

The following are new or modified grounds of rejection necessitated by Applicant's Amendment, filed 28 Apr 2008, in which claims 2, 11 and 16-19 are canceled; claims 1 and 10 are amended to change the scope and breadth of the claim; and claims 3, 12 and 13 are amended so as not to depend from a canceled claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Amended Claims 1, 3-10 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takahashi et al. (WIPO publication WO 02/36135, published 10 May 2002, of record) and Bowman et al. (WIPO publication WO 00/69441, published 23 Nov 2000, of record), which is incorporated-by-reference into Takahashi et al.

(Takahashi et al. page 1, lines 5-7) in view of Dorr et al. (Cancer Chemotherapy Handbook, 1994, Appleton & Lange, 2nd ed, p395-416, of record).

Takahashi et al. discloses the method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma (page 2, lines 26-29), specifically envisioning treating a human (page 4, lines 11-12). Takahashi et al. specifically references WO 00/69441 (Bowman et al.) for dosing schemes for ET-743 (page 5, lines 12-13). Bowman et al. discloses the recommended doses for ET-743 of 500 micrograms per m^2, or 0.5 mg/m^2 (Bowman et al. page 13, lines 16-17 and 20-21). The method of combination therapy of ET-743 and doxorubicin to treat the cancer sarcoma in a human 0.5 mg/m^2 doses for ET-743 meets limitations of instant claims 1, 14 and 15. Takahashi et al. discloses the drugs provided as a separate composition for administration at different times (page 1, lines 12-13), meeting limitations of instant claim 3. Takahashi et al. discloses administering ET-743 after administering doxorubicin (page 21, lines 13-14), which is to say administering doxorubicin prior to the administration of ET-743, meeting limitations of instant claim 4. Takahashi et al. discloses administration of the compounds by intravenous infusion, with infusion times of up to 24 hours and 2-6 hours preferred (page 4, lines 25-26), meeting limitations of instant claims 5-7. Compared to an infusion time of 24 hours, 2 hours is about 1 hour or 3 hours. Takahashi et al. discloses infusions carried out at suitable intervals of 2 to 4 weeks (page 5, lines 2-3), anticipating instant claim 8. Takahashi et al. specifically references WO 00/69441 (Bowman et al.) for dosing schemes for ET-743 (page 5, lines 12-13). Bowman et al. discloses administration of ET-734 performed in cycles of 3 weeks, or 21 days, with the

drug administered in the first days of each cycle, and schedule adjustments performed as needed depending on the individual patient (Bowman et al. page 12, lines 1-6), meeting limitations of instant claims 9 and 10. Takahashi et al. discloses the correct dosage of the compounds will vary according to the particular formulation, mode of application, *situs*, host, and tumor being treated (page 5, lines 6-10), meeting limitations of instant claims 12-13. Bowman et al., incorporate-by-reference into Takahashi et al., discloses the recommended doses for ET-743 of 0.5 mg/m^2 (Bowman et al. page 13, lines 16-17 and 20-21), which when compared a dose of 1.65 mg/m^2 disclosed by Bowman et al. is about 0.6 mg/m^2 or about 0.7 mg/m^2, meeting limitations of instant claims 12 and 13.

Takahashi et al. does not specifically disclose doxorubicin administered with a dose of about 60 mg/m^2 or about 50 mg/m^2, disclosed in instant claim 1. Takahashi et al. does not specifically disclose the infusion of doxorubicin carried out once every 21 days, disclosed in instant claim 9. Takahashi et al. does not specifically disclose the method wherein the infusion of doxorubicin is carried out on day 1 and the infusion of ET-743 on days 1 and 8, every 21 days, disclosed in instant claim 10.

Dorr et al. teaches dosing guidelines for doxorubicin of 60-75 mg/m^2 administered every 3 weeks (page 399, table on lines 38-45), or 21 days. Compared to a dose of up to 120 mg/m^2 (page 399, left column, lines 10-13), a dose of 60 mg/m^2 is about 50 mg/m^2.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Takahashi et al. using the dosage of doxorubicin of

about 60 mg/m^2 or about 50 mg/m^2 administered every 3 weeks taught by Dorr et al. Dorr et al. teaches guidelines for dosing, which would motivate one of ordinary skill in the art at the time of the invention to follow the guidelines. Takahashi et al. discloses the correct dosage of the compounds will vary according to the particular formulation, mode of application, *situs*, host, and tumor being treated (page 5, lines 6-10). Bowman et al. discloses administration of ET-734 performed in cycles of 3 weeks, or 21 days, with the drug administered in the first days of each cycle, and schedule adjustments performed as needed depending on the individual patient (Bowman et al. page 12, lines 1-6). Therefore one of ordinary skill in the art at the time of the invention would be motivated to practice the method wherein the infusion of doxorubicin is carried out on day 1 and the infusion of ET-743 on days 1 and 8, every 21 days.

Response to Applicant's Remarks:

Applicant's Amendment and Remarks, filed 28 Apr 2008, have been fully considered and not found to be persuasive.

Applicant asserts that one of ordinary skill in the art would not combine Dorr with Takahashi because Dorr teaches said dosage amounts of doxorubicin as a single agent. However, Dorr does teach the administration of doxorubicin with other agents, such as other anthracyclines or DNA-intercalating compounds, which the dose limit must take into account (page 399, right column, paragraph 4) due to having the same mechanism of action (page 396, left column, paragraph 3). However, D'Incalci et al. (The Oncologist, 2002, 7, p210-216, cited in PTO-892), provides evidence of the state of the art at the time of the invention and indicates that the mode of action of ET-743 is

unique and that "it possesses antitumor activity against tumors that are refractory to standard anticancer drugs, all of which certainly act by mechanisms that are different from that of ET-743." (abstract). Therefore, one of ordinary skill in the art at the time of the invention would have a reasonable expectation that an agent that has a mechanism of action that is certainly different from doxorubicin, such as ET-743, would not affect the dose limit of doxorubicin. One of ordinary skill in the art, having an expectation that the dose limit would not be affected, would look to the dosage amount of the single agent doxorubicin as guidance for the dosage for doxorubicin in combination with an agent that has a different mechanism of action. Therefore, in view of the state of the prior art and the teachings therein, Applicant's assertion that the results of the instantly claimed invention are unexpected is not persuasive.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended Claims 1 and 3-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 and 19-20 of commonly assigned copending Application No. 11/577,790.

Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-11 and 19-20 of copending Application No. 11/577,790 are drawn to a method of treating cancer in a human comprising administering ET-743 and a Pegylated Liposomal form of the anthracycline Doxorubicin. Instant claims 1 and 3-9 are drawn to the method of treating cancer in a human comprising administering ET-743 and doxorubicin. The instant specification discloses one non-limiting embodiment wherein the doxorubicin does not take the form of doxorubicin in the Pegylated Liposomal form (page 8, lines 8-10). However, this disclosure leads one to immediately envision the opposite, the embodiment wherein the doxorubicin does take the form of doxorubicin in the Pegylated Liposomal form. Claims 2 and 3 recites the limitation of instant claim 3. Claim 4 recites the limitation of instant claim 4. Claim 5 recites the limitation of instant claim 5. Claim 6 obviates the limitation of instant claim 6. Claim 7 obviates instant claim 7. Claim 8 obviates instant claims 8 and 9. Claims 10 and 11 obviates the dosage ranges of instant claim 1. Instant claim 2 discloses the method wherein doxorubicin is administered with a dose of 40 mg/m^2, which is about 30 mg/m^2 when compared to the disclosed value of 80 mg/m^2, obviated by the doxorubicin dosage of claim 11 of copending Application No. 11/577,790.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claim is found to be allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jonathan S. Lau whose telephone number is 571-270-3531. The examiner can normally be reached on Monday - Thursday, 9 am - 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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